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Early intervention in psychosis: keeping faith with evidence-based health care

A commentary on: 'Early intervention in psychotic disorders: faith before facts?' by Bosanac *et al.* (2009)

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Introduction

As a group of clinical researchers committed not only to the principles of evidence-based health care but also to the creation and translation of new knowledge to the community, we are grateful for the opportunity to respond to Bosanac *et al.* (2009). Although Bosanac *et al.* do not initially seem to be disputing the aims of early intervention (EI), they go on to embark upon a selective critique of its concepts and targets. The main complaint seems to be that new investment in specialized EI services diverts funding from mainstream services. This premise creates a false dichotomy, pitting the value of EI against the legitimate need of the persistently mentally ill for ongoing care.

Bosanac *et al.* have set themselves a difficult challenge in attempting to defend mainstream generic care as a viable alternative to specialized youth and family-friendly care for emerging and early psychosis. Generic services all around the world are characterized by long delays in treating patients for the first time (Norman & Malla, 2001; Farooq *et al.* 2009). Furthermore, once access is achieved, the experiences of patients and relatives in these settings are traumatic, demoralizing and aversive, leading to high rates of disengagement (Garety & Rigg, 2001). Such services tend to concentrate on acute crises and risk management alone rather than on recovery, constrained as

they are by meagre resources and heavy stigma. If their paper is dissected carefully, it is possible to distil Bosanac *et al.*'s main criticisms of EI, which will be considered below.

EI services are skewed towards managing 'easy' patients

Under the section 'Caseness in early psychosis' and again in the section 'The DUP conundrum', Bosanac *et al.* claim that EI services manage patients with psychotic disorders 'that are by their very nature more transient and more amenable to intervention' and that have 'an inherent tendency to better outcomes'.

The EI field is indeed aiming to focus on the early stages of psychotic disorder by minimizing the duration of untreated illness. This is consistent with a staging approach (McGorry *et al.* 2006), enabling treatment of illness that is intrinsically more likely to be responsive to safer treatments (not necessarily antipsychotic medications) and to minimize the need for traumatic and restrictive forms of care, including involuntary hospitalization. This does not mean that the disorders are inherently likely to have a better outcome. The focus is the early stage of disorder. In line with traditional psychiatric thinking dating back to the Kraepelinian era, Bosanac *et al.* believe that there are essentially two classes of patients. The first group have an essentially trivial problem, a kind of noisy phenocopy that superficially resembles schizophrenia, for which specialist care is unnecessary and a misuse of resources. The second group are an intrinsically

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doomed group of unfortunates with 'real schizophrenia' who can expect an inevitably poor outcome, despite treatment, but nevertheless should not be 'medicalized' until it is clear that they are well on the way to, or indeed have already arrived at, this self-fulfilling fate. Bosanac *et al.* imply that EI services show good outcomes because they mainly treat these 'easy' patients. Yet they later assert that there is no evidence for the effectiveness of EI services. This seems to contradict their first point. Nonetheless, we will endeavour to deal with each assertion in turn.

It seems that Bosanac *et al.* want to be sure that it is the people with 'real schizophrenia' – those who fulfil DSM-IV criteria B (marked social deterioration) and C (duration of illness of at least 6 months) for schizophrenia – who receive services. Yet the requirement of these criteria encourages delayed intervention and is harmful to health (McGlashan *et al.* 2007). Delaying intervention until an individual has deteriorated and has chronic entrenched illness results in a host of secondary morbidity as the individual may engage in highly visible uncontrolled and stigmatizing behaviour, family and peers are alienated, substance abuse accelerates and vocational, educational and personality development is disrupted. Suicide is a serious risk. As Lieberman & Fenton (2000) stressed: 'psychosis damages lives'. Additionally, prolonged duration of untreated psychosis (DUP) is associated with poor outcome, an issue we deal with in more detail later.

Furthermore, contrary to Bosanac *et al.*'s assertions, most cases in first-episode psychosis services fall within the existing schizophreniform/schizophrenia categories. The benefits of specialized treatment models are evident. For example, in the OPUS study, where the duration of untreated psychosis (DUP) was substantial, there was still significant early benefit derived from more specialized early care (Petersen *et al.* 2005). Similarly, in the TIPS project there was evidence of additional and more enduring benefits from earlier detection of those with schizophrenia spectrum disorders (Melle *et al.* 2009). Both early detection and assured specialized treatment are important elements.

EI services 'over-medicalize' problems

Confusingly, in their section on 'The Duration of Untreated Psychosis conundrum' and again in their section on 'The problem of labelling, and potential treatment-related harm', Bosanac *et al.* discuss some of the issues involved in identification and treatment of young people at risk of psychotic disorder but who are not yet psychotic. We have previously developed criteria for identifying individuals with an increased risk

of onset of psychotic disorder within the near future, the 'ultra-high-risk' (UHR) criteria (Yung *et al.* 2003, 2004). They are largely identified by the presence of subthreshold psychotic symptoms. Despite repeatedly confusing this pre-psychotic stage of disorder with the later stage of sustained full threshold psychosis, Bosanac *et al.* do raise some issues that need to be addressed. However, far from being at risk of 'over-medicalization', young people seeking help in the UHR phase present with genuine symptoms, distress and deterioration. They have been shown to be at very high risk (a relative risk of 405; Cannon *et al.* 2008) for transition to sustained psychotic disorder, with early transition rates from the UHR state to first-episode psychosis of between 10% and 50% reported (for a review, see Olsen & Rosenbaum, 2006).

The need for care typically precedes the emergence of sustained positive psychotic symptoms in those who develop schizophrenia and other psychotic illnesses (Yung & McGorry, 1996; Hafner, 2000). Contrary to Bosanac *et al.*'s assertion, many of these help-seeking patients have experienced lengthy periods of symptoms and have made more than one contact with services (Phillips *et al.* 1999). Although it is true that there is a significant 'false positive' rate for transition to psychosis, provided sustained distress, impairment and help-seeking are evident, these criteria clearly identify a clinical sample at substantial risk for persistence of, or progression to, a range of disabling mood disorders, including the psychotic disorders (Yung *et al.* 2004). There is therefore a case to be made for widening the focus of the UHR criteria with features aiming to capture incipient risk for severe mood disorders. This should be progressed in stigma-free youth-friendly environments.

Bosanac *et al.* assume that the interventions proposed for the UHR group involve the inevitable use of antipsychotic medications. On the contrary, we are clear that such use is not yet supported by sufficient evidence to suggest that the benefits outweigh the risks. The international clinical guidelines for early psychosis (International Early Psychosis Association Writing Group, 2005) are conservative, reflecting international agreement that antipsychotic medications should not be a first-line treatment, and stress psychosocial and other more benign strategies within a stepped care algorithm. There is indeed a need for more randomized controlled trials (RCTs), especially of putative neuroprotective agents. However, the need for a more extensive evidence base should not disqualify those with both the need and the desire for care from access to treatment based on the best available evidence. This is currently only possible within low-stigma specialized clinics or youth mental health models of care (McGorry *et al.* 2007).

Bosanac *et al.* rightly point out that psychotic-like symptoms are more common in the general population than we previously thought, often without an apparent need for care (van Os *et al.* 2001, 2009; Scott *et al.* 2006; Yung *et al.* 2009). It would indeed be to be harmful to label these otherwise well individuals as mentally ill and to 'pathologize normal developmental processes'. We have previously pointed this out, and noted that psychotic-like experiences are likely to be heterogeneous in aetiology (Yung *et al.* 2009). The challenge is to distinguish between those in the community whose symptoms are likely to resolve or cause them no harm, and those in whom the psychotic-like symptoms presage serious mental disorder. Several of us are actively involved in research addressing this issue. One factor that increases the risk of psychotic-like experiences requiring treatment is distress (Hanssen *et al.* 2005). Poor functioning is also likely to identify those at risk of further deterioration. Finally, help-seeking is a crucial factor. UHR (or 'prodromal') services do not screen adolescents in school and compel them to attend for treatment. They offer a service to help-seeking, distressed individuals whose psychotic symptoms would be considered too mild for mainstream services, but who nonetheless have genuine mental health problems.

'The extent to which DUP independently predicts outcomes remains a problem'

The serious mismatch between resources and need for care, existing in all countries (Prince *et al.* 2007), means that, far from over-medicalization, most people are denied access or gain it only after substantial delay. Reducing DUP is in no way dependent on progress with prodromal or UHR case definition. We are on firm terrain here in seeking to reduce the period of potentially life-threatening untreated full-blown psychotic illness. The link between DUP and outcome is no longer a 'vexing' issue because the relationship between treatment delay and poor outcome has been clearly established (Marshall *et al.* 2005; Perkins *et al.* 2005). This has now been confirmed in low- and middle-income countries (Farooq *et al.* 2009). Research from Canada and the UK has shown that much of the treatment delay occurs *after* help-seeking and *within* generic services, strongly supporting the need for specialized pathways and clinical service systems for early psychosis (Norman *et al.* 2004). Furthermore, the TIPS study has shown that not only is it possible to substantially reduce DUP through community education and mobile detection teams but also the risk of suicidal behaviour is reduced, and even longer DUP cases of schizophrenia are identified with higher Global Assessment of Functioning (GAF) scores (Melle

et al. 2004). These patients are in 'better shape' at entry to care with much less 'collateral damage' than would otherwise have been the case (Friis *et al.* 2005). So the potentially poor prognosis cases *are* detected, engaged and treated earlier and more effectively than in generic models. A somewhat longer period of follow-up is needed to confirm that this is not merely a 'zero time shift phenomenon'. In fact, even though DUP is only a proximal risk factor for outcome, in the TIPS study reductions in DUP have been associated with sustained positive effects on 5-year outcome, including negative symptoms (Melle *et al.* 2009). These sustained benefits of reducing DUP underline the importance of striving for full remission *after* entry to care so the total duration of active psychosis is minimized.

EI services are not effective

This is the crux of the matter. Although health services research is challenging, some ground-breaking work has been done that shows that specialized streams of care for early psychosis clearly open up a differential outcome trajectory. A recent meta-analysis shows a distinct advantage for specialized EI services over standard care during the first 12 months of care (Harvey *et al.* 2007) and several lines of evidence, not merely RCTs, all point in the same direction. Current guidelines (e.g. www.nice.org.uk) endorse early psychosis intervention models. Furthermore, two service-level RCTs have demonstrated the advantages of EI for up to 2 years post-diagnosis (Craig *et al.* 2004; Petersen *et al.* 2005; Garety *et al.* 2006). For example, the OPUS trial (Bertelsen *et al.* 2008) found that those accessing EI services had greater rates of independent living and reduced homelessness; improved psychotic symptoms; lower levels of substance abuse; and better global functioning at 2 years' follow-up. Bosanac *et al.* question these findings on the grounds that assessors of outcome were not blinded. Although we agree that future studies should aim to blind raters as much as possible (albeit a difficult task), lack of blinding is most unlikely to be a complete explanation for the differences, as some of these outcomes are 'hard' findings that would not be affected by blinding raters (living arrangements, vocational outcomes and service contacts and engagement, for example).

One mechanism through which EI services work is obvious and does not require dismantling strategies. Young people engage better in such models of care and are therefore much more likely to receive and adhere to interventions necessary for recovery. By contrast, generic services have very high rates of disengagement, with patients twice as likely to disengage (Craig *et al.* 2004). Indeed, retention of first-episode cases is not even a goal of most generic services.

EI services retain close to 80% of all cases over the first 2 years (Schimmelmann *et al.* 2006) and the treatment components are linked to the needs and stage of illness. These better outcomes are even seen when DUP has not been reduced at all (Petersen *et al.* 2005). Suicide rates are lower in specialized early psychosis programmes as long as such optimistic and assured care is available (Harris *et al.* 2008). When patients are transferred too soon to the pessimism of generic services, for many there is a rebound effect on suicide rates (Harris *et al.* 2008). There is a dramatic cost-effectiveness advantage of early psychosis programmes such that the annual cost of direct mental health care is one-third that of care provided in generic systems (Mihalopoulos *et al.* 2009). In addition, vocational recovery is much more effective when provided to patients at this stage of illness than in late-stage patients (Killackey *et al.* 2008).

Bosanac *et al.* are essentially defending a generic model of care, one that currently offers little more than acute containment and palliative care and that has been heavily criticized by consumers and carers (Rethink, 2003). By contrast, EI services are extremely popular with consumers (Lester *et al.* 2009).

Bosanac *et al.* are correct in pointing out that, although some studies show maintenance of early gains (Melle *et al.* 2009; Mihalopoulos *et al.* 2009), when EP care is prematurely withdrawn from a substantial subset of cases there may be a tendency for some of these gains to be lost (Bertelsen *et al.* 2008). This is something that also concerns us. Unfortunately, it seems that reducing DUP and providing specialized services may not substantially benefit some patients. There may be some individuals who develop poor outcomes despite optimal treatment in an EI service, which, while disease modifying, is not curative *per se*. A challenge is to identify which patients do best and how to maintain these gains, and to identify those manifesting early non-response, a secondary early intervention focus. The development of better interventions for these 'EI non-responders' is needed.

In addition, it may be that some individuals require a longer period of specialized care, perhaps up to 5 years rather than the 18 months to 2 years generally funded now. We saw, for example, in the OPUS trial that although some gains were preserved, some seemed to be eroded at the 5-year follow-up (though loss of power may have been a factor) after patients had been transferred for 3 years to generic services. Clearly, 2 years of specialized early psychosis care may have been too little for some patients. The Gafoor *et al.* (2008) study also suggested this, although the authors freely acknowledged that it was too underpowered to tell whether the earlier benefits of the early psychosis service had in fact 'disappeared'. However,

if the findings of these longer-term follow-up studies are at least partially valid, then what they in fact demonstrate is the inability of generic services to maintain hard-won gains and underlines their inherent weakness. In sum, it is likely that the timing, nature, quality and duration of treatment for early psychosis are all important. Current evidence suggests that many patients benefit from specialized services, making the difference between a life of disability and a life of relatively high functioning. For some, the effects may not be as profound. Nonetheless, early detection of non-response may be useful, and these non-responders may still have gain from family involvement, psychological support and knowing they were afforded optimal care. Clearly, more research is needed to address how long specialized treatment needs to continue and to investigate different therapeutic options; but it would be irresponsible to dismiss lightly, as do Bosanac *et al.* the current evidence for the effectiveness of EI.

Conclusions

Developmental sensitivity and EI are extremely difficult features to embed in a 'one size fits all' adult psychiatry. The creation of a first generation of early psychosis models has been a significant advance that has enabled crucial evidence to be amassed. However, this has only occurred in some countries and typically to a limited extent. Much more substantial worldwide investment is now justified and is indeed being undertaken in many jurisdictions. This ultimately has the potential to lead to truly stigma-free mental health care for a broader range of young people with emerging mental disorders (McGorry *et al.* 2007).

Although practical problems associated with early diagnosis are raised in other areas of health care, the fundamental value of the endeavour is not repeatedly questioned as we have seen in mental health. Beginning with vision, logic and 'faith', any innovation has to pass through a series of steps before it becomes part of the accepted landscape of care, and EI is well down the track (McGorry *et al.* 2008). As it is strongly supported by the 'facts', the concept has been endorsed by policymakers, clinicians and research leaders alike (Insel, 2009). We agree that it is not Emil Kraepelin who deserves censure, but those who cling to an approach that has passed its 'use-by date' and that causes real harm to patients by delaying care and manufacturing a hopelessness that is by no means justified by the facts or by sensible clinical strategy. Fortunately, in Australia (paradoxically the source of the Bosanac *et al.* editorial), the National Health and Hospitals Reform Commission has recently endorsed youth-friendly mental health care and the national

roll-out of specialized early psychosis services as the top two out of 12 recommendations for national mental health reform (National Health and Hospitals Reform Commission, 2008).

The questioning of cherished assumptions and evidence is at the heart of science and we welcome the opportunity to engage in this debate. We trust that the authors are likewise also willing to question their assumptions and provide evidence for maintaining the status quo. It is curious that in psychiatry we often miss the big picture. It would be surprising in the fields of cancer or cardiovascular medicine to find the professional leadership canvassing arguments that would justify delaying treatment for potentially life-threatening conditions. Critics should always be asked to nominate how much delay they personally find acceptable after psychotic symptoms, distress and functional impairment have emerged and been sustained in a young person. It is a matter of common sense that seriously ill people should have the pathway to care eased, not blocked. Early psychosis programmes create such pathways and safeguard tenure in care. We are unapologetic in demanding better services and resources for people with psychosis during all its stages throughout the lifespan.

Declaration of Interest

None.

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